1: Development. 1995 Jun;121(6):1787-99.

Zebrafish wnt8 and wnt8b share a common activity but are involved in distinct developmental pathways.

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The specification of the vertebrate body plan is dependent on numerous signaling molecules, including members of the Wnt family. We have identified two zebrafish wnt8 paralogs related to Xwnt-8B and Xwnt-8, respectively. A RT-PCR assay demonstrated that wnt8 is expressed maternally, with transcripts detected throughout embryogenesis, whereas wnt8b transcripts were first detected during late gastrulation. The wnt8 transcripts at 50% epiboly are spatially restricted to those cells at the blastoderm margin, overlying gsc-expressing cells in the axial hypoblast. During late gastrulation, wnt8 was no longer detected in the marginal cells at the dorsal midline and by mid-segmentation, transcripts were found in the presumptive tail bud. In contrast, wnt8b expression is spatially restricted to prospective neuroepithelium, and later to neural-specific structures. Overexpression of both wnts results in two major phenotypes: radialized embryos and embryos with anterior defects. These phenotypes were preceded by significant changes in the spatial expression patterns of gsc and ntl transcripts, reminiscent of activities of Xwnt-8 in Xenopus, and consistent with a role for wnt8 in the specification or patterning of mesoderm.

PMID: 7600994 [PubMed - indexed for MEDLINE]

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1: Mech Dev. 1998 Feb;71(1-2):119-29.

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BMP-2/-4 and Wnt-8 cooperatively pattern the Xenopus mesoderm.

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Establishment of the dorsoventral axis is central to animal embryonic organization. In Xenopus two different classes of signaling molecules function in the dorsoventral patterning of the mesoderm. Both the TGF-beta-related products of the BMP-2 and BMP-4 genes and the Wnt molecule encoded by Xenopus Wnt-8 specify ventral fate and appear to inhibit dorsal mesodermal development. The similar functions of these molecularly very different classes of signaling molecules prompted us to study their mutual regulation and to closely compare their roles in mesoderm patterning. We find that Wnt-8 and BMP-4 are indistinguishable in their abilities to induce expression of ventral genes. Although BMP-2/-4 signaling regulates Wnt-8 expression, these genes do not function in a linear pathway because Wnt-8 overexpression cannot compensate for an inhibition of BMP-2/-4 function, but rather BMP-4 overexpression rescues ventral gene expression in embryos with inhibited Wnt-8 function. We further find that Wnt-8 and BMP-2/-4 differ in their abilities to regulate dorsal gene expression. While BMP-4 appears to generally inhibit the expression of dorsal genes, XenopusWnt-8 only inhibits the expression of the notochord marker Xnot. Whereas the inhibitory effect of BMP-2/-4 localizes dorsal mesodermal fate, our results suggest that Xenopus Wnt-8 functions in the further patterning of the dorsal mesoderm into the most dorsal sector from which the notochord develops and the dorsolateral sector from where the somites differentiate.

PMID: 9507084 [PubMed - indexed for MEDLINE]

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1: Development. 1998 Nov;125(21):4283-92.

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Evidence for a frizzled-mediated wnt pathway required for zebrafish dorsal mesoderm formation.

Nasevicius A, Hyatt T, Kim H, Guttman J, Walsh E, Sumanas S, Wang Y, Ekker SC.

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We have used zebrafish as a model system for the study of vertebrate dorsoventral patterning. We isolated a maternally expressed and dorsal organizer localized member of the frizzled family of wnt receptors. Wild-type and dominant, loss-of-function molecules in misexpression studies demonstrate frizzled function is necessary and sufficient for dorsal mesoderm specification. frizzled activity is antagonized by the action of GSK-3, and we show GSK-3 is also required for zebrafish dorsal mesoderm formation. frizzled cooperatively interacts with the maternally encoded zebrafish wnt8 protein in dorsal mesodermal fate determination. This frizzled -mediated wnt pathway for dorsal mesoderm specification provides the first evidence for the requirement of a wnt-like signal in vertebrate axis determination.

PMID: 9753682 [PubMed - indexed for MEDLINE]

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1: Genes Dev. 1999 Dec 1;13(23):3149-59. Related Articles, Links

Wnt signaling in Xenopus embryos inhibits bmp4 expression and activates neural development.

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We report a new role for Wnt signaling in the vertebrate embryo: the induction of neural tissue from ectoderm. Early expression of mouse wnt8, Xwnt8, beta-catenin, or dominant-negative GSK3 induces the expression of neural-specific markers and inhibits the expression of Bmp4 in Xenopus ectoderm. We show that Wnt8, but not the BMP antagonist Noggin, can inhibit Bmp4 expression at early gastrula stages. Furthermore, inhibition of beta-catenin activity in the neural ectoderm of whole embryos by a truncated TCF results in a decrease in neural development. Therefore, we suggest that a cleavage-stage Wnt signal normally contributes to an early repression of Bmp4 on the dorsal side of the embryo and sensitizes the ectoderm to respond to neural inducing signals from the organizer. The Wnt targets Xnr3 and siamois have been shown previously to have neuralizing activity when overexpressed. However, antagonists of Wnt signaling, dnXwnt8 and Nxfrz8, inhibit Wnt-mediated Xnr3 and siamois induction, but not neural induction, suggesting an alternative mechanism for Bmp repression and neuralization. Conversely, dnTCF blocks both Wnt-mediated Xnr3 and neural induction, suggesting that both pathways require this transcription factor.

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